TEMPORAL AND FREQUENCY ANALISYS OF CLICK-EVOKED OTOACOUSTIC EMISSIONS RECORDED FROM UNTREATED CONGENITAL HYPOTHYROID NEWBORNS.

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Abstract- **Thyroid hormone plays an important role in hearing development. The exact incidence of hearing impairment in untreated congenital hypothyroid newborns (CH) is unknown. This paper presents the results of the measuring of the transient-evoked otoacoustic emissions (TEOAE) on a population of 29 newborns positive to the screening test for hypothyroidism. TEOAE were recorded in all newborns in 1 month after birth and before starting the L-thyroxin treatment. We performed both temporal and time-frequency analysis of the responses by means of Wavelet transform. 68 newborns who had no risk factor for hearing loss served as control. The comparison of the characteristics of temporal and frequency content of the responses of the two groups showed no statistically significant difference (p=0.01).**

Keywords **- Hypothyroidism; newborns; transient-evoked otoacoustic emissions; Wavelet transform.**

I. Introduction

Congenital hypothyroidism is a common disease with an incidence of 1 in every 4000-5000 newborns [3]. The thyroid hormone (TH) is necessary for a normal development of the auditory system[16]: both a genetic or acquired neonatal thyroid hormone deficiency may result in a profound mental disability that is often accompanied by deafness. The associations between thyroid disorders and auditory system dysfunction has been identified in both animal models and human patients [2-5;7-8;12;15].

However, the exact incidence of hearing impairment in untreated congenital hypothyroid (CH) newborns is still unknown as well as the direct action of thyroxin on the peripheral hearing organs in humans.

The purpose of this study was to analyse the effects of thyroid hormone deficiency on the peripheral auditory system in humans. Transient evoked otoacoustic emissions (TEOAE), were used to test the micromechanical activity of the outer hair cells of the cochlea. In fact TEOAE are acoustic signals emitted by the cochlea and reflect the active processes that are involved in the transaction of mechanical energy into electrical energy [6]. One of the features of the TEOAE is their tight relation to the cochlea status: TEOAE are universally present to a various degree in all healthy cochleae, whereas they are not generally observed or are greatly reduced in ears with mild hearing losses.

In this study, analysis of the time-frequency properties of the TEOAE is therefore used to monitor the cochlear functionality and to compare the characteristics of the waveforms recorded from two population (CH and control).

II. Methodology

Transient evoked otoacoustic emissions (TEOAE) were recorded using a probe inserted into the outer ear canal. The probe contains a miniaturised microphone and a transmitter that delivered the acoustic stimulus. In the present study 29 CH newborns (54 ears), born between August 1997 and April 2000 and identified through the thyroid screening program implemented at the San Raffaele Hospital in Milan, were tested with TEOAE before starting the L-thyroxin treatment. 68 well babies (100 ears), randomly chosen from all the newborns included in the Hearing Screening Program of the San Raffaele Hospital in Milan, were used as control group.

The test was performed in all newborns (control and CH) in 1 month after birth at the most. TEOAE were recorded using a standard ILO88 system (Otodynamic Ltd.). Responses were filtered with the ILO88 default procedure (second-order high pass filter set at 330Hz, gain 1.57 and fourth-order low pass set at 10.6 kHz, gain 2.6) and digitalized at a rate of 25.000 samples/s. Responses to 260 repetitions of the click-train (four clicks per train) were averaged according to the “non-linear” mode of operation (i.e. a train of three clicks followed by a fourth click of inverse polarity and three times greater; this method takes advantage of the nonlinear behaviour of the TEOAE) in the *QuickScreen* acquisition mode with a sweep time of 12.5 ms. Finally, average data were digitally filtered off-line (second order digital bandpass set at 600÷6000 Hz).

In all the recording sessions, the click-stimulus level ranged from 77 to 83 dB SPL and two replicates (A and B) of the responses were collected in the same recording conditions.

As to the PASS/FAIL criteria, a TEOAE response was scored as PASS when the total reproducibility was equal to or greater than 70%, and the reproducibility equal to or greater than 50% in the 1.5 kHz band and 70% in 2.2, 3.0 and 3.7 kHz bands was found. When the stimulus stability i.e. an estimate average correlation between the waveforms of the stimulus at the beginning and at the end of the recording, was lower than 70%, the recording is scored as FAIL (technical fail).

Both temporal and frequency content of the whole set of evoked responses that passed the TEOAE test (31 ears of the CH newborns and 100 ears of the control newborns), were analysed.

A. Time-amplitude analysis

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For all subject, the root mean square value (RMS) of the average between A and B replicates was computed. The RMS of a discrete signal which consists of N equispaced samples *x(n)* is given by (1):

$$x_{rms} = \sqrt{1/N \cdot \sum_{n=1}^{N} x(n)^2} \quad (1)$$

In this investigation, RMS amplitude was computed in 11 subwindows; the duration of each subwindow was set at 4 ms, with a temporal overlap of 3 ms. The first and the last windows started at 6 and 16 ms, respectively. Thus, for each emission, eleven values in time were obtained, which can be considered as the RMS relative to the mean value of the extremes of the temporal moving window. Also the RMS amplitude of the noise was estimated. An estimate of the noise was obtained considering the difference in the two replicate responses, A and B, divided by root 2, in order to take into account both constructive and destructive effect of the noise components on the recording [10].

B. Wavelet approach

The Wavelet Transform is a linear time-frequency distribution which decomposes a signal into a family of basis function:

$$WT(\bar{t}, f) = \int_t x(t)\sqrt{f / f_o} \cdot h^*((f / f_o)\cdot(t-\bar{t}))dt \quad (2)$$

The basis function $\sqrt{f / f_o} \cdot h((f / f_o(t))$ are scaled and shifted version of the same prototype function *h(t)*, the mother wavelet. *h(t)* is a function with finite energy and centered around time t=0; its FT is a bandpass function centered around frequency f_o. The Wavelets have a constant relative bandwidth, i.e. the quality factor Q (center frequency/bandwidth) is constant. Unlike STFT, time and frequency resolution are not fixed over the entire time-frequency plane: time resolution becomes good at higher frequencies whereas frequency resolution becomes good at lower frequencies. The particular structure of the wavelet filters (narrow bandwidth and long duration for low-frequency filters; broad bandwidth and brief duration for high-frequency filters) makes the WT approach highly suitable for signals with low-frequency components of long duration and high frequency components of brief duration as the TEOAE.

In this study the time-frequency Continuous Wavelet Transform was computed using as mother wavelet *h(t)* the temporal function:

$$h(t) = \frac{\cos(bt)}{1+t^m} \quad (3)$$

as suggested by Tognola [13]where *b* was set to 20 and *m* to 8. Time *t* and frequency f parameters were sampled using a uniform sampling grid: t=*n*T and f=*k*F, where T is the sampling period in time (0.04 ms), F is the step in frequency (500 Hz) and *n*, *k* are integers. We utilised a technique, based on the inverse WT, to decompose emissions into elementary components[13-14], on the basis of the spectral properties of band-pass filters of WT. For all responses, the frequency contents of the average of the A and B replicates were analysed in 8 frequency bands (from 1750 to 5250 Hz, step 500 Hz). Decomposition of TEOAE into elementary components could be useful to study the characteristics of each components and to compare the differences between the hypothyroid and the control group. In particular, the RMS, the latency and the reproducibility were investigated.

The root mean square (RMS) of each frequency component for all subjects was computed from the average of A and B replicates using a rectangular windows from 0.04 to 20.44 ms; the latency is defined as the time interval from the stimulus onset to the maximum of the envelope of the frequency component considered; the reproducibility is defined as the zero-lag correlation between A and B frequency components, computed in the temporal window from 6 to 18 ms, to avoid the influence of the initial artefact .

C. Statistical analysis

A statistical analysis was applied to the results of the study of the amplitude (RMS) over frequency and time, of the latency and of the reproducibility over frequency. Statistical analysis was performed by the Group Comparison t test, if the observed samples came from a population with a normal distribution, or by the Wilcoxon test, if the observed samples didn't come from a normal distribution. In both case the level of significance was set to a probability of 0.01.

III. RESULTS

23 ears (42,6%) out of the 54 who were tested from the CH newborns failed the TEOAE test according to the PASS/FAIL criteria described before. This result showed an increase in the population of newborns classified as fail compared with the average data of the hearing newborns screening program implemented at San Raffaele Hospital in Milan.

In fig.1 the average across all the ears of the RMS amplitude of the TEOAE classified as PASS recorded from the two group is presented as a function of the post-stimulus time; the two functions are nearly superimposed along all the post-stimulus time. The RMS amplitude of the noise level is on average 53% of the RMS amplitude of the TEOAE.

In fig.2 the average RMS amplitudes is presented as a function of frequency. The RMS amplitude of the control group is greater than the one of the CH newborns in all the frequency bands.

In fig. 3 the average latency is presented as a function of frequency. It is to notice that the two functions are nearly superimposed in all the frequency bands.

In fig.4 the reproducibility is presented as a function of frequency. The reproducibility of the control group is always lower than the one of the CH group, especially in the frequencies below 3.5 kHz.

The statistical analysis applied to the temporal (RMS versus post-stimulus time) and frequency (RMS, onset latency and reproducibility versus frequency) characteristics of the responses of the two groups (CH and control) showed no statistically significant difference (p=0.01) in all the temporal windows and in all frequency bands.

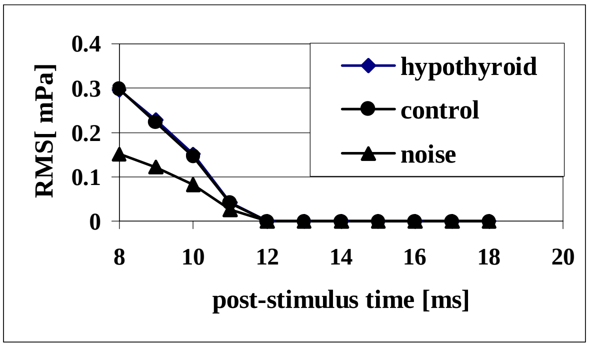

Fig.1. TEOAE amplitude recorded form CH and control newborns. RMS value are computed in 11 temporal windows, 4 ms long and shifted on 1 ms. The first window is centred at 8 ms (i.e. it starts at 6 ms and ends at 10 ms). The curves shows the results of the average of all ears .

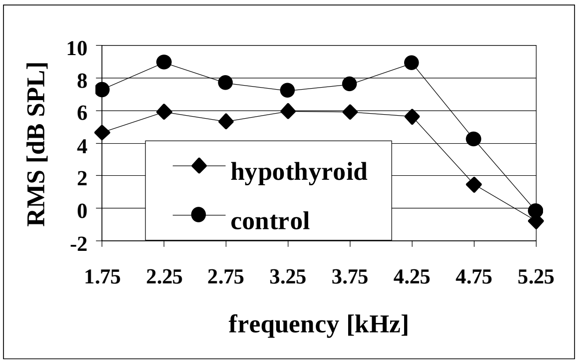

Fig.2 Frequency components amplitude of TEOAE recorded form CH and control newborns. RMS value of each components are computed using a temporal window of 20.40 ms. The curves shows the result of the average of all the ears.

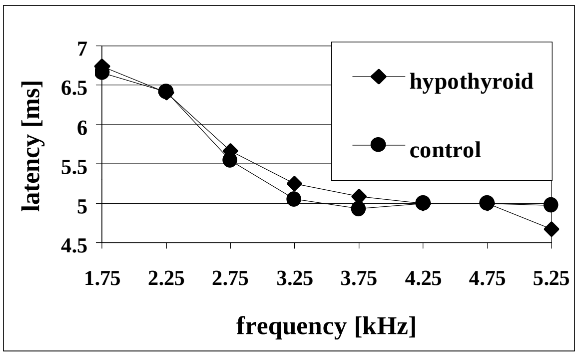

Fig.3 Frequency components latency of TEOAE recorded from CH and control group. The curves shows the results of the average of all the ears.

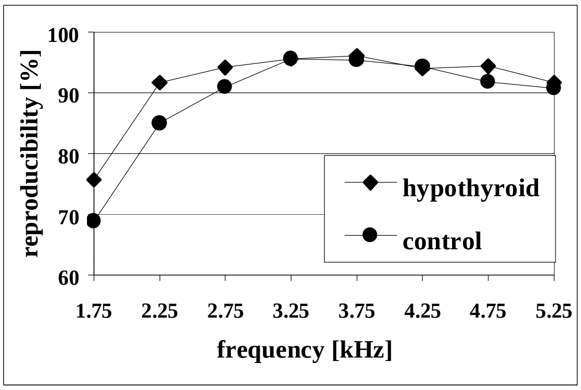

Fig.4 Frequency components reproducibility of TEOAE recorded form CH and control newborns. The curves shows the results of the average of all the ears.

IV. CONCLUSION

Time-frequency analysis of TEOAE by wavelet transform can be considered a useful tool to study the physiologic effect of thyroid hormone depletion on hearing and the function of outer hair cell. In fact the particular structure of the TEOAE requires a method able to discriminate both high-frequency components of brief duration and low-frequency components of long duration. The WT seems to be the best compromise between time-frequency resolution and interference term attenuation. The analysis of TEOAE could therefore provide indirect information on outer hair cell function that is not available from ABR and electrocochleography. In fact, otoacoustic emissions are thought to reflect the activity of active biological mechanisms within the cochlea responsible for the exquisite sensitivity, sharp frequency selectivity and wide dynamic range of the normal auditory system. It is now accepted that the OHC system is responsible for the generation of otoacoustic emission and that OHC motility is the cellular basis for this phenomenon [1].

In our investigation, no statistically significant differences were found between the CH and control TEOAE properties (RMS, latency, reproducibility) both in temporal (11 subwindows from 6 ms to 16 ms) and frequency (8 frequency bands from 1750 to 5250 Hz, step 500 Hz) domain. Our results seems to suggest that in humans, the deficiency of thyroxin during the phase of maturation of the cochlea couldn't influence the normal biological activity of the OHC. Moreover, this could suggest that the development of the cochlea is little sensitive to fetal hypothyroidism, or that the level of circulatory thyroid hormone in these newborns during fetal life is sufficient for normal development. According to other authors [4] there could be some transfer of maternal thyroid hormone to the fetus. This might explain why our results in CH newborns differ from those reported in experiments with animals, where tectorial membrane irregularity and outer cell damage were found.

As to the PASS/FAIL criteria, the results of this study seem to indicate that there is a decrease of the signal-to-noise ratio of the responses of the CH newborns compared with the average data of the local newborns screening program. This produces an increase in the CH population of the newborns classified as fail

No correlation between congenital hypothyroidism and congenital deafness was found apart from the fact that 7 CH newborns who failed the TEOAE test, showed a decrease of the diameter of the epiphisary distal nuclei of the femur.

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REFERENCES

[1] W.E Brownell, "Outer hair cell electromotility and otoacoustic emissions," *Ear. Hear*, vol.11, pp.82-92,1990.

[2] F. Debruyne, Vanderschueren-Lodeweyckx, P. Bastijns, "Hearing in congenital hypothyroidism", *Audiology*,vol. 22,pp.404-409,1983.

[3] D.A. Fisher, J.H Dussault, J.P. Foley, A.H. Klein, S.L. LaFranchi, P.R. Larsen, "Screening for congenital hypothyroidism: Results of screening one million North American Infants", *J. Pediatr*,vol. 94,pp. 700-705, 1979.

[4] M.Francois, P. Bonfils, J. Leger, P. Avan, P.Czernichow, P.Narcy, "Audiological Assessment of eleven congenital hypothyroid infants before and after treatment", *Acta Otolaryngol*,vol.113,pp.39-42, 1993.

[5] M. Francois, P. Bonfils, J. Leger, P. Czernichiw, P. Narcy, "Role of congenital hypothyroidism in hearing loss in children", *J. Pediatr*,vol.124,pp.444-446, 1994.

[6] D.T. Kemp, "The evoked cochlear mechanical response of the auditory microstructure in models of the auditory system and related signal processing techniques", *Scandinavian Audiology*, vol.9,pp.35-47,1979.

[7]W.L Meyerhoff, "Hypothyroidism and the ear: electrophysiological, morpological and chemical considerations", *Laryngoscope*,vol. 89,pp.1-25,1979.

[8]B.W. O'Malley, D. Li,D. S. Turner, "Hearing loss and coclear abnormalities in the congenital hypothyroid (hyt/hyt) mouse" *Hear Res.*,vol.88,pp.181-189,1995.

[9]P. Ravazzani, G. Tognola, F. Grandori, "Derived nonlinear versus linear click-evoked otoacoustic emissions" *Audiology*,vol.35,pp.73-86,1996.

[10]P. Ravazzani, G. Tognola, F. Grandori, "Optimal bandpass filtering of transient-evoked otoacoustic emissions in neonates", *Audiology*,vol.38,pp.69-74,1999.

[11]O. Rioul, M.Vetterli, "Wavelet and signal processing", *IEEE SP Magazine October*,pp.14-45,1991.

[12]J.Rovet, W. Walker, B. Bliss, L. Buchanan, R. Enrlich, "Long-term sequelae of hearing impairment in congenital hypothyroidism", *J. Pediatr.*, vol. 128,pp. 776-783,1996.

[13]G. Tognola, F. Grandori, P. Ravazzani, "Time-frequency distributions of click-evoked otoacoustic emissions", *Hear. Res.*,vol.106,pp.112-122,1997.

[14]G. Tognola, F. Grandori, P. Ravazzani, "Wavelet analysis of click-evoked otoacoustic emissions", *IEEE transaction on biomedical engineering*,vol.45 (6),pp.1-12,1988.

[15]A. Uziel, J. Gabrion, M. Ohresser, C. Legrand, "Effects of hypothyroidism on the structural development of the organo del Corti in the rat", *Acta Otolaryngol.*, vol. 92 (5-6),pp.469-80,1981.

[16]H.P. Wit, P. Van Dijk, P. Avan, "Wavelet analysis of real and synthesised click evoked otoacoustic emissions", *Hear. Res.*, vol. 73,pp.437-445,1994.